reported in the largest study (N = 407; p < 0.01). In four studies reporting total gastrointestinal (GI) AE data, donepezil was consistently associated with a lower incidence of GI AEs compared to rivastigmine, with three of these reporting a lower incidence for donepezil compared to galantamine. In the largest study reporting total GI AEs (N = 5462), the incidence was donepezil 6%, rivastigmine 14%, and galantamine 24%. In all studies, low numbers of CNS and cardiovascular AEs were recorded, with similar incidences of events found across the different AChEIs. **CONCLUSIONS:** In routine clinical settings, mild to moderate AD patients who received donepezil had fewer total and GI AEs versus patients treated with rivastigmine or galantamine.

PMH5

USING TREEMAPS TO ASSESS PHYSICAL COMORBIDITY RISK IN PATIENTS WITH BIPOLAR DISORDER

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OBJECTIVES: Research has shown bipolar patients are at greater risk for somatic illnesses than the rest of the population. This study assesses the incidence and relative risk (RR) of physical comorbid disease among patients with bipolar disorder. **METHODS:** A large US longitudinal claims database and medical episode grouping software was used to construct disease specific episodes of care for the years 2006–2007. The case population consisted of individuals <65 years with an episode of bipolar disorder and at least 12 months of continuous enrollment (CE). The control population were year-, age- and sex-matched individuals with no mental health or substance abuse episodes and at least 12 months CE. A total of 102,670 cases and 205,340 controls were matched for the year 2006; 109,124 cases and 218,248 controls were matched in 2007. Treemaps produced by SAS v. 9.1 are used to convey the relative rankings of disease incidence and RR of disease as compared to persons without mental health disorders. **RESULTS:** Compared to controls, cases had elevated RR of disease ranging from 1.25 (conditions of the female reproductive system) to 3.14 (trauma or iatrogenic conditions). Among the specific trauma and iatrogenic conditions, poisoning, adverse drug reactions and injury the RRs at least 2.5 times higher than controls. Cases had a RR of 1.69 for endocrine and metabolic diseases (e.g diabetes, hypothyroidism, hypoglycemia). Musculoskeletal conditions and ear, nose and throat conditions were the most common types of physical comorbidities among both cases and controls, however, RR was 1.59 times higher for cases. **CONCLUSIONS:** Compared to patients with no mental health diagnoses, patients with bipolar disorder are at greater risk for a wide range of physical comorbidities. Treemaps are a valuable tool for visualizing the relative impact of a broad range of diseases across two populations.

PMH6

IMPACT OF COMORBIDITIES ON ANTIDEPRESSANT INITIATION: DULOXETINE, VENLAFAXINE, AND ESCITALOPRAM VERSUS OTHER SSRIS

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OBJECTIVES: Although efficacy and safety are 2 key issues to be taken into account when choosing an antidepressant, many other factors may also influence treatment initiation. The purpose of the study was to examine the impact of comorbidities on the initiation of antidepressants: duloxetine (DLX), valenfaxine (VLX), and escitalopram (ECP) versus other SSRIs (OSSRI) in patients with major depressive disorder (MDD). **METHODS:** A total of 44,026 MDD patients from a large commercial administrative claims database were classified as initiators of DLX (n = 7,567), VLX (n = 6,106), ECP (n = 10,239), or OSSRI (n = 20,114) during the year 2006. Patients were classified on their first index medication during the study period. All patients had no active prescription of the same medication(s) in the prior 3 months. On the basis of ICD-9-CM, 17 systemic disease classes and 21 individual diseases in the prior 12 months were identified. **RESULTS:** Patients receiving DLX were more likely than those receiving VLX, ECP, and OSSRI to be female (75.1% vs. 71.5%, 69.7%, 70.5%, p < 0.001) and aged 46 years or above (62.3% vs. 54.6%, 49.8%, 50.5%, p < 0.001). Nearly all systemic disease classes and individual pain diseases were most prevalent in DLX patients, followed by VLX and ECP patients, with OSSRI patients being the least. Most significant predicting comorbid diseases (OR > 1.40) of DLX initiation versus OSSRI were fibromyalgia (OR = 1.86), low back pain (OR = 1.54), and bipolar disorder (OR = 1.43) after adjustment for demographics and other comorbidities. However, no comorbid diseases with an OR > 1.40 were associated with VLX and ECP initiation versus OSSRI. **CONCLUSIONS:** Patients initiating DLX have the most comorbid diseases, followed by VLX, ECP, with patients initiating OSSRI having the least. Specifically, the presence of chronic pain diseases and bipolar disorder appear to be most significant predictors of DLX initiation relative to OSSRI.

PMH7

EFFICACY OF ANTIPSYCHOTICS IN THE PREVENTION OF SCHIZOPHRENIA RELAPSE: A SYSTEMATIC REVIEW OF DOUBLE BLIND RANDOMISED CONTROLLED TRIALS

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OBJECTIVES: Conduct a systematic review in schizophrenia relapse prevention, using the same methodology as the recent National Institute for Clinical Excellence (NICE) Schizophrenia Clinical Guideline. **METHODS:** Systematic review of CENTRAL, EMBASE, MEDLINE, for double-blind RCTs with, amisulpride, aripiprazole, olanzapine, paliperidone, quetiapine, risperidone, ziprasidone or zotepine, (completed November 2008). Relapse and withdrawal data were extracted using individual trial definitions. Mixed treatment comparison using Markov Chain Monte Carlo simulation was conducted using a random effects model to estimate the risk of relapse, treatment discontinuation due to either intolerable adverse effects (DAE) or other reasons. Summary effect estimates are presented as Odd Ratios [OR] with 95% Credible Intervals (95%CrI) calculated versus placebo. **RESULTS:** Literature searching returned 488 papers that identified 18 RCTs that were of sufficient quality to be included in the analysis. Relapse analysis reported quetiapine (XR) followed by risperidone and zotepine as most effective: quetiapine (XR) (OR: 0.151, 95%CrI: 0.021, 0.52), risperidone (OR: 0.168, 95%CrI: 0.035, 0.52), zotepine (OR: 0.17, 95%CrI: 0.017, 0.69), olanzapine (OR: 0.225, 95%CrI: 0.081, 0.513), haloperidol (OR: 0.314, 95%CrI: 0.075, 0.89), ziprasidone (OR: 0.315, 95%CrI: 0.079, 0.85), paliperidone (OR: 0.362, 95%CrI: 0.058, 1.214), amisulpride (OR: 0.387, 95%CrI: 0.041, 1.497), aripirazole (OR: 0.518, 95%CrI: 0.09, 1.702). Amisulpride, olanzapine and ziprasidone reported lowest OR for DAE. Amisulpride, quetiapine (XR) and olanzapine reported lowest OR for withdrawal due to other reasons, respectively. The model was considered a good fit for relapse and discontinuation due other reasons but not for DAE. **CONCLUSIONS:** When NICE's schizophrenia guideline was in production, quetiapine (XR) was not licensed in the UK and therefore excluded from the health economic model. However, it is now available and the above analysis suggests that treatment with quetiapine (XR) could potentially provide benefit in the management of schizophrenia relapse prevention. No firm conclusions can be made from the analysis DAE.

PMH8

CLINICAL EFFICACY AND SAFETY OF DULOXETINE IN COMPARISON WITH PLACEBO IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER IN POLAND

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OBJECTIVES: The objective of this analysis was to compare efficacy and safety of duloxetine with placebo in the treatment of major depressive disorder in Poland. **METHODS:** Comparison was based on a systematic review, carried out according to guidelines published by the Cochrane Collaboration and the Agency for Health Technology Assessment in Poland. The most important medical databases (MEDLINE, EMBASE, CENTRAL) were searched. Two reviewers independently had selected trials, assessed their quality and extracted data. For efficacy analysis improvements in Hamilton Rating Scale for Depression (HAM-D) and quality of life were measured. Percentage of patients responding to treatment (defined as ≥50% improvement in HAM-D) and percentage of patients achieving total remission (defined as ≤7 points HAM-D-17) were also reported. Head-to-head comparisons based on randomized controlled trials (RCTs) were performed both for safety and efficacy analysis. **RESULTS:** The results of 14 RCTs were included in the analysis. After 7 to 9 weeks of treatment duloxetine allowed better improvement than placebo in HAM-D scores (WMD = −2.26 [−2.94; −1.57]) and in quality of life (WMD = −3.60 [−4.89; −2.31]). Percentage of patients with response to treatment (RB = 1.42 [1.29; 1.56]), NNT = 6.95 [5.53; 9.37]), and with total remission (RB = 1.45 [1.29; 1.64]), NNT = 8.92 [6.80; 12.93]) was also statistically significantly higher for duloxetine group. Although risk of adverse events was significantly higher in duloxetine treated patients (RR = 1.19 [1.13; 1.24]; NNH = 8.60 [6.75; 11.84]), no differences in the incidence of serious adverse events were observed (RR = 0.95 [0.49; 1.84]). Withdrawals due to adverse events were significantly more frequent in duloxetine group than in placebo group (RR = 2.11 [1.61; 2.77], NNH = 17.31 [12.87 26.44]). **CONCLUSIONS:** Duloxetine is efficacious drug in the treatment of patients with major depressive disorder. Safety profile seems to be acceptable (slightly worse than placebo).

PMH9

A SYSTEMATIC REVIEW OF PHARMACOLOGICAL TREATMENTS FOR BIPOLAR I MANIA

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OBJECTIVES: Update a previously published systematic review[1] of pharmacological treatments for acute mania in bipolar I disorder, to include recent publications, including new formulation quetiapine extended release (XR), and remission rates. **METHODS:** Systematic review of CENTRAL, EMBASE, MEDLINE, for randomised, controlled trials comparing placebo to: aripiprazole, carbamazepine, divalproex, haloperidol, lithium, olanzapine, quetiapine XR, and risperidone as monotherapy, in the treatment of acute mania in bipolar I disorder, published before March 2009. Trials of combination therapy and patients non-responsive to previous therapy were excluded. Data were combined through random effects meta-analyses using Comprehensive Meta Analysis. Summary effect estimates were presented as Relative Risk (RR) versus placebo and 95% Confidence Interval (95%CI). **RESULTS:** 408 publications were identified and overall 19 trials from 18 papers were included in the analysis. The results for remission reported that risperidone followed by quetiapine XR were the most effective antipsychotics: risperidone (RR:1.87, 95%CI:1.22–2.85), quetiapine XR (RR:1.46, 95%CI:1.07–2.01), olanzapine (RR:1.39, 95%CI:1.08–1.79),

aripiprazole (RR:1.29, 95%CI:1.05–1.58), haloperidol (RR:1.29, 95%CI:1.03–1.62). Lithium followed by divalproex ER were the most effective mood stabilisers: lithium (RR:1.73, 95%CI:1.08–2.79), divalproex ER (RR:1.40, 95%CI:1.09–1.80), divalproex (1.12, 95%CI:0.81–1.55), carbamazepine ER (not available). The results for response reported that risperidone and quetiapine XR were the most effective antipsychotics: risperidone (RR:1.77, 95%CI:1.50–2.09), quetiapine XR (RR:1.61, 95%CI:1.23–2.10), olanzapine (RR:1.54, 95%CI:1.23–1.92), aripiprazole (RR:1.46, 95%CI:1.26–1.70), haloperidol (RR:1.41, 95%CI:1.19–1.66). Carbamazepine ER followed by lithium were the most effective mood stabilisers: carbamazepine ER (RR:2.01, 95%CI:1.55–2.61), lithium (RR:1.57, 95%CI:1.28–1.92), divalproex (RR:1.46, 95%CI:1.10–1.93), divalproex ER (RR:1.45, 95%CI:1.12–1.87). Due to incomplete reporting, the pooled mean difference in YMRS was considered unreliable. **CONCLUSIONS:** Selecting the right pharmacological treatment strategy which optimises remission is key to maximising patient outcomes and efficient use of health care resources. This analysis suggests that risperidone, quetiapine XR and lithium are promising treatment options for bipolar I mania. 1. Smith, Bipolar Disord. 2007;9:551–560.

PMH10

EFFECTIVENESS AND COST-EFFECTIVENESS OF LIFESTYLE INTERVENTIONS IN PERSONS WITH SEVERE MENTAL DISORDERS. A SYSTEMATIC REVIEW

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OBJECTIVES: When compared to the general population, people with severe mental disorder (SMD) more commonly show obesity, sedentary lifestyles and poor dietary choices. This review examines the effectiveness and cost-effectiveness of lifestyle interventions on physical activity and dietary choices in people with SMD. Included health outcomes were changes in weight, body mass index (BMI) and quality of life. **METHODS: A systematic E-search strategy was conducted** using Medline, Web of Science and CINAHL to select articles of lifestyle interventions targeting exercise and dietary choices in people with SMD. In addition, the reference lists of retrieved articles from the E-databases were hand-searched. **RESULTS:** The search strategy produced 14 randomized and non-randomized comparative trials that met the inclusion criteria. Mean duration of the interventions was 20.0 ± 10.84 weeks. Weight loss was reported in 11 studies, with a mean weight change of −1.96 ± 1.84 kg in the intervention groups versus +1.77 ± 2.12 **kg in the control groups.** Changes in BMI were −0.87 ± 0.69 **kg/m² and** +0.64 ± 0.96 **kg/m² respectively in** intervention and control groups. Differences in changes in weight and BMI between intervention and control groups were statistically significant in nine studies. The results also suggest that quality of life and general health could benefit from these kinds of interventions. For example, subjective improvements in quality of life ($p = 0.047$) and in overall health ($p = 0.023$) were found in the study of Evans et al. (2005). In none of the studies, however, cost-effectiveness was examined. **CONCLUSIONS:** Small weight loss through lifestyle interventions targeting physical activity and dietary choices is possible in people with SMD. This is promising given the high prevalence of sedentary lifestyles and poor dietary choices and the effects of some atypical antipsychotics on weight gain. Further study of both effectiveness and cost-effectiveness (including the most cost-effective 'dose') of lifestyle interventions in people with SMD is required.

PMH11

DIFFERENCES BETWEEN CHILDREN AND ADOLESCENTS IN TREATMENT RESPONSE TO ATOMOXETINE AND THE CORRELATION BETWEEN QOL AND ADHD CORE SYMPTOMS

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OBJECTIVES: To explore differences between age subgroups in QOL in atomoxetine treated patients and evaluate correlations between ADHD core symptoms and QOL. **METHODS:** Pooled data of 5 similar clinical atomoxetine trials (8–12 weeks follow-up, 3 placebo-controlled, 2 open-label) were included in the analysis. All studies used the ADHD-RS and the CHIP-CE instruments. Treatment group differences (effect size vs. placebo) in CHIP-CE score changes were compared between different age groups (< /&GE;12YRS); > **RESULTS:** A total of 611 children (<12 yrs) and 183 adolescents (≥12 yrs) were included. Baseline CHIP-CE total t-scores (mean ± SD; norm: 50 ± 10) were similar in children (29.3 ± 11.58) and adolescents (27.5 ± 12.29) ($p = 0.296$). Greater impairments in the CHIP-CE 'achievement' domain were seen in adolescents than children (t-scores 31.0 ± 10.26 and 28.9 ± 10.71, respectively; $p < 0.05$); there were no clinically relevant differences in other domains. For the CHIP-CE 'risk avoidance' domain, the effect size of atomoxetine was higher in adolescents than in children (0.83, $p < 0.001$ and 0.37, $p = 0.005$; age*treatment interaction $p = 0.059$); age group differences for other domains and CHIP-CE total scores were not clinically relevant. ADHD-RS/CHIP-CE correlations were low at baseline but moderate for change from baseline being similar in age groups. Only the 'risk avoidance' domain showed a trend towards lower correlation of change in adolescents ($r = -0.384$ and $r = -0.545$). **CONCLUSIONS:** Both age groups showed a clinically relevant impairment of QoL at baseline which was similar for adolescents and children in four out of five CHIP-CE domains. In both groups, atomoxetine was effective in improving QoL. For the 'risk avoidance' domain, the effect size of atomoxetine was larger in adolescents than in children, while the ADHD-RS/CHIP-CE correlation was lower in adolescents, indicating a lower association with core symptoms.

PMH12

COMPARISON OF POLYPHARMACY VS MONOTHERAPY ON OCCURRENCE OF RELAPSE IN SCHIZOPHRENIC PATIENTS – ADVANTAGE OF PROPENSITY SCORING ADJUSTMENT

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OBJECTIVES: The objective was to compare occurrence of relapse according to antipsychotic treatment (monotherapy vs polypharmacy), in a 2 year observational cohort of 288 French schizophrenic patients, using different methods of adjustment. **METHODS:** Relapse was defined by a usual, clinically well reproducible and validated definition. The occurrence of relapse between patients receiving one antipsychotic to patients receiving more than one antipsychotic was compared according to a Cox model including or not the propensity score (PS). The propensity score was calculated on socio-economic and demographic information, clinical variables, quality of life, medication information and attitude toward treatment. Cox models were built according to four usual methods to calculate the propensity score: 1—stepwise PS, continuous, 2—non stepwise PS, continuous, 3—non stepwise PS, quintiles 4—non stepwise PS quintiles used to stratify the sample. We also used standard adjustment using all variables included in the model estimating the PS. Likelihood, *Akaike's* information criterion (AIC) criterion and Schwatz's Bayesian *Criterion* (SBC) criterion were used to compare the models. **RESULTS:** The standard cox model reports significant decrease of relapse in patient receiving polytherapy. Consistently the four models based on propensity scoring methods did not find any difference between the two populations. The model that optimizes all criteria (−2logL, AIC and SBC) is the model using the stratification on the propensity score. **CONCLUSIONS:** Polytherapy is not associated to a reduction of relapse while consistently literature reports major risk associated to polypharmacy including increased mortality. The use of propensity scoring is well established for observational data and this study illustrate that standard regression could be misleading.

PMH13

TIME TO OPTIMIZATION OF DOSE IN PATIENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD): DATA FROM THE NETHERLANDS

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OBJECTIVES: To evaluate time to optimization of dose in children with ADHD in The Netherlands. **METHODS:** Claims data from the PHARMO medical record linkage system database from 48 geo-demographic areas in The Netherlands (2003–2006) were analyzed from newly treated ADHD patients aged 6–17 years. Patients were followed for at least 12 months after treatment initiation with methylphenidate or atomoxetine. Demographic and medication characteristics at treatment initiation, and concurrent psychotropic treatments in the year before ADHD treatment initiation were recorded. For this analysis, only patients with ³5 dispensings for any ADHD drug during follow-up and no missing information on type of drug, strength, and number of pills per day were included. Optimized dosing regimen was defined as no change in type of drug, strength, and number of pills per day for 5 consecutive dispensings (no time restriction between dispensings). Time to optimized dosing regimen was defined as the number of days between the first dispensing for an ADHD drug (cohort entry date) and the first of five unchanged dispensings. **RESULTS:** Of 4909 children initiating treatment from 2003–2006, 3159 met selection criteria. The proportion of patients reaching dosing optimization with initial treatment was 69.8% for atomoxetine (ATX; n = 37), 74.8% for short-acting methylphenidate (SA; n = 2017), and 82.4% for long-acting methylphenidate (LA; n = 262; $P < 0.05$ for both ATX and SA vs LA). The median number of days required to reach optimal dosing regimen was 49 across the total sample. Among patients achieving dose optimization, those initiating treatment with LA had a significantly shorter time to dose optimization (14 days) than patients initially treated with SA (56 days; $P < 0.001$) or ATX (31 days; $P < 0.05$). **CONCLUSIONS:** Time to optimization of dosing regimen in children with ADHD in The Netherlands varied according to treatment chosen at initiation and was shortest for long-acting methylphenidate. Supported by funding from Shire Development Inc.

PMH14

ALZHEIMER'S DISEASE: A PHARMACOEPIDEMIOLOGICAL STUDY

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OBJECTIVES: Alzheimer's disease is an irreversible progressive disease that affects cognitive, behavioural and functional abilities. The prevalence of Alzheimer's disease is increasing as the world's population is aging. The primary aim of the study was to determine the prescribing patterns and cost of drugs for Alzheimer's disease in a private health care sector patient population. **METHODS:** A retrospective, exposure-cohort pharmacoepidemiological study was conducted. Data were obtained from a South African private pharmacy group for 2008. The database consisted of 1,578,346 medicine records. **RESULTS:** A total of 588 patients (326 females and 262 males) received 2623 medicine items for Alzheimer's disease at a cost of R1,563,701.18 (average cost per item R596.15). The average age of patients was 75.54 (SD = 10.48) years, with 78.40% of patients between 70 and 89 years of age. Donepezil was the most frequently prescribed active ingredient (37.09%), followed by galantamine (36.94%). Donepezil accounted for 39.50% of the cost of Alzheimer medication. No notable differences in prescribing patterns were observed over the 12-month period.